Bilateral Vision Loss Associated With Cryptococcal Meningitis
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Abstract:
AIDS patient presents with acute bilateral blindness, central scotomas, and cryptococcal meningitis. DFE, OCT, and ERG show no ocular pathology. MRI shows normal optic nerves and atypical cortical blindness resulting from cryptococcal damage is presumed.

I. Case History
1) Patient demographics: 46 year old African-American male.
2) Chief complaint: Severe vision loss OU over the course of several weeks.
3) Ocular history: Mild myopia.
4) Medical history: HIV x 12 years. Patient presented to ER six weeks prior to presentation in eye clinic with complaints of headaches and fever. His blood and CSF tested positive for *cryptococcus neoformans* confirming cryptococcal meningitis. At that presentation his CD4 count was 23.
5) Medications: HAART with a history of non-compliance. At the initial diagnosis of cryptococcal meningitis in the ER the patient was treated with IV amphotericin B and flucytosine until he was afebrile and CSF cultures came back negative for organisms. At that point he was switched to oral fluconazole 400mg daily and discharged from hospital thereafter. Following discharge the patient was non-compliant with his oral fluconazole as well.
6) Other salient information: Patient reports severe headaches in occipital region of skull occurring almost every day over the several weeks prior to presentation in the eye clinic. Patient also has history of polysubstance abuse and homelessness.

II. Pertinent findings
1) Clinical: Presenting BCVA was 20/400 OU with eccentric fixation. Intraocular pressures, extra ocular motilities, and pupillary testing were all normal. Slit lamp exam and dilated fundus exam revealed no ocular pathology. Confrontation visual field testing and Goldmann visual field (GVF) testing revealed small dense central scotomas in both eyes. These scotomas were repeatable on subsequent GVF testing, were five to ten degrees round, and were consistent with the loss of macular function in both eyes (Image 1). OKN drum testing was unresponsive in primary gaze but present and appropriate with eccentric fixation. Optical coherence tomography of the maculae and retinal nerve fiber layers were unremarkable in both eyes. Electroretinogram studies of both the scotopic and photopic pathways where normal confirming a healthy functioning retina (Image 2). Visually evoked potential testing is scheduled to be performed and results should be available in the near future.
2) Physical: The patient also developed severe bilateral hearing loss suggesting a deficit in the eighth cranial nerves. The results of an audiology consult are pending.
3) Laboratory studies: Following presentation in the eye clinic the patients CD4 count was low at 88 cells per micro-liter and HIV viral load was high at 39,500 copies per mL. He had elevated brain natriuretic peptide levels. Lumbar puncture (LP) opening pressure was 4.1 cmH2O and cerebrospinal fluid was positive for *cryptococcus neoformans*.
4) Radiology studies: MRI studies showed no pathology of the optic nerves or orbit (Image 3). There was thickening with increased enhancement involving the meninges and cranial nerves at
the basal cisterns and base of the brain which was radiographically consistent with meningitis. Thickening of the 5th, 8th, and 9th cranial nerve meninges was noted. Multiple focal areas of abnormal signal intensity without mass effect were scattered throughout the brain including the brainstem and basal ganglia. None of the lesions demonstrated enhancement after the administration of gadolinium contrast material. These lesions were consistent with the radiologic appearance of cryptococcomas suggesting deep cortical invasion by the cryptococcal organism (Image 4).

5) Others: The patient is scheduled for an audiology consult and test results will be forthcoming.

III. Differential diagnosis
1) Primary/leading: The most commonly noted cause of vision loss in cryptococcal meningitis is infectious optic neuropathy secondary to direct invasion of the optic nerve and meninges. This mechanism is usually seen in acute cases of vision loss over the course of several days. The second most common cause of vision loss in cryptococcal meningitis is elevated CSF pressure, usually with a papilledematous appearance of the ONH which is cited in cases of vision loss over the course of several weeks. In this case, however, fundus examination and MRI reveal no involvement of the optic nerves. The pattern of the central scotomas seem to correlate with bilateral damage to the posterior aspect of the occipital lobe. Furthermore, the presence of presumed cryptococcomas seen on the MRI scans suggest deep invasion of the cryptococcal organism into cortical tissue. Thus, a differential diagnosis of presumed atypical cortical blindness due to direct invasion of the cryptococcal organism into the occipital lobe must be considered. VEP testing will help to support or contradict the diagnosis of presumed cortical blindness. This test should prove useful because the pattern of visual field loss is consistent with loss of macular function and the VEP signal is dominated by the macula. It must also be noted that the VEP is dependent on proper conduction of the retrobulbar optic nerve and although structural measures have indicated there is no optic nerve pathology it is possible that acute inflammation of the nerves occurred and subsided before MRI was performed. If pallor of the ONH develops in the coming weeks/months the diagnosis of infectious optic neuritis will be more likely. The patient is also undergoing a series of therapeutic LPs and if this is shown to reduce vision loss then the CSF pressure mechanism will be more likely.
2) Others: Non-organic vision loss such as hysterical blindness is unlikely as the GVF are highly repeatable.

IV. Diagnosis and discussion
1) Elaborate on the condition: Cryptococcal meningitis is an infection of the meningial tissues by the fungal pathogen Cryptococcus neoformans. This infection occurs in immunocompromised patients and is very rare in patients who are not immunocompromised. Of all HIV/AIDS patients 6-7% will have cryptococcal meningitis throughout the course of their disease. In HIV/AIDS vision loss occurs in 1-5% of all cases of cryptococcal meningitis. Cryptococcal meningitis also carries a high mortality rate at 10-30%, making it the fourth most common source of life-threatening infection found in HIV/AIDS. The typical mechanisms of vision loss in cryptococcal meningitis were outlined above.
2) Expound on unique features: Vision loss in cryptococcal meningitis is typically seen with direct infectious optic neuritis or increased CSF pressure resulting in papilledema. This case is unique in that the patient presents dense central scotomas without any structural signs of
pathology involving the optic nerves. Due to the absence of optic nerve pathology and the presence of presumed cryptococcomas on MRI, one must consider the possibility that direct cryptococcal invasion into cortical tissue could be the cause of vision loss here.

V. Treatment, management
1) Treatment and response to treatment: The patient was again treated with IV amphotericin B and flucytosine until switched to oral fluconazole which is the standard of care. Subsequent LPs continued to show high opening pressures but subsequent cultures and stains showed no organisms in the cerebrospinal fluid. Vision loss has remained stable without improvement and no ocular pathology has developed. The hearing loss has continued to progress. The patient is currently undergoing a series of therapeutic LPs, this is the only treatment in the literature that has shown positive results in halting or reversing vision loss in cryptococcal meningitis. Oral acetazolamide to manage CSF pressure has shown to be less effective and lumbar drainage shunts carry higher risks in immunocompromised patients. LV devices and eccentric fixation training has been provided to the patient.

2) Research/Literature review/ Bibliography: References are attached at the end of the outline and the findings in research and review of the literature are mentioned in the discussion and treatment sections of this outline.

VI. Conclusion
In a patient who has HIV/AIDS or is immunocompromised with acute vision loss cryptococcal meningitis must be placed on the list of differential diagnoses and ruled out, especially in the presence of no perceived ocular pathology.

References

Y Hong et al. Complete binocular blindness as the first manifestation of HIV-related cryptococcal meningitis. Journal of clinical neurology. 2007: 3 (4); 212-214.


O Torres et al. Visual loss due to cryptococcal meningitis in AIDS patients. AIDS. 1999: 13 (4); 530-534.


Image 1: Goldman Visual fields showing dense bilateral central scotomas.

Image 2: Normal ERG studies. (Higher quality image will be available for final presentation)
Image 3: MRI showing no optic nerve pathology.
Image 4: MRI showing presumed cryptococcoma lesion.